

CLAIMS

What we claim is:

1. An isolated *Listeria* bacterium which is attenuated for entry into non-phagocytic cells and comprises a nucleic acid molecule encoding a non-Listerial antigen.
2. The attenuated *Listeria* bacterium of claim 1, which is further attenuated for cell-to-cell spread.
3. The attenuated *Listeria* bacterium of claim 2, which comprises at least one mutation in one or more gene selected from the group consisting of *actA*, *lplA*, *plcA*, *plcB*, *mpl* and *hly*.
4. The attenuated *Listeria* bacterium of claim 3, which comprises a mutation in *actA*.
5. The attenuated *Listeria* bacterium of claim 2, wherein nucleic acid of the bacterium has been modified by reaction with a nucleic acid targeting compound so that proliferation of the bacterium is attenuated.
6. The attenuated *Listeria* bacterium of claim 5, wherein nucleic acid of the bacterium has been modified by contact with a psoralen activated by UVA irradiation.
7. The attenuated *Listeria* bacterium of claim 1, which is defective with respect to one or more internalins.
8. The attenuated *Listeria* bacterium of claim 7, which is defective with respect to internalin B.
9. The attenuated *Listeria* bacterium of claim 8, which comprises a mutation in the *inlB* gene.

10. The attenuated *Listeria* bacterium of claim 8, which is further attenuated for cell-to-cell spread.
11. The attenuated *Listeria* bacterium of claim 10, which is defective with respect to ActA.
12. The attenuated *Listeria* bacterium of claim 11, which comprises at least one mutation in both *actA* and *inlB*.
13. The attenuated *Listeria* bacterium of claim 1, which belongs to the species *Listeria monocytogenes*.
14. The attenuated *Listeria* bacterium of claim 1, wherein the antigen is a tumor-associated antigen or derived from a tumor-associated antigen.
15. The attenuated *Listeria* bacterium of claim 14, wherein the antigen is a tumor associated antigen or derived from a tumor associated antigen selected from the group consisting of mesothelin, sp17, PAGE-4, gp-100, PSMA, K-ras, TARP, proteinase 3, WT-1, NY-ESO-1, CEA, Her-2, and SPAS-1.
16. The attenuated *Listeria* bacterium of claim 1, wherein the antigen is an infectious disease antigen or is derived from an infectious disease antigen.
17. The immunogenic composition comprising the attenuated *Listeria* bacterium of claim 1.
18. A vaccine comprising (a) the attenuated *Listeria* bacterium of claim 1, and (b) a pharmaceutically acceptable carrier or adjuvant.
19. A method of inducing an immune response in a host to a non-Listerial antigen comprising administering to the host an effective amount of a composition comprising the attenuated *Listeria* bacterium of claim 1.

20. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a composition comprising the attenuated *Listeria* bacterium of claim 1.
21. A professional antigen-presenting cell comprising the attenuated *Listeria* strain of claim 1.
22. An isolated *Listeria* bacterium which is attenuated both for entry into non-phagocytic cells and for cell-to-cell spread.
23. The attenuated *Listeria* bacterium of claim 22, which comprises at least one mutation in one or more gene selected from the group consisting of *actA*, *lplA*, *plcA*, *plcB*, *mpl* and *hly*.
24. The attenuated *Listeria* bacterium of claim 23, which comprises a mutation in *actA*.
25. The attenuated *Listeria* bacterium of claim 22, wherein nucleic acid of the bacterium has been modified by reaction with a nucleic acid targeting compound so that proliferation of the bacterium is attenuated.
26. The attenuated *Listeria* bacterium of claim 25, wherein nucleic acid of the bacterium has been modified by contact with a psoralen activated by UVA irradiation.
27. The attenuated *Listeria* bacterium of claim 22, wherein the attenuated *Listeria* bacterium is defective with respect to one or more internalins.
28. The attenuated *Listeria* bacterium of claim 27, which is defective with respect to internalin B.
29. The attenuated *Listeria* bacterium of claim 28, which comprises at least one mutation in the *inlB* gene.

30. The attenuated *Listeria* bacterium of claim 28, which is defective with respect to ActA.
31. The attenuated *Listeria* bacterium of claim 30, wherein the attenuated *Listeria* bacterium comprises at least one mutation in both *actA* and *inlB*.
32. The attenuated *Listeria* bacterium of claim 22, which belongs to the species *Listeria monocytogenes*.
33. The attenuated *Listeria* bacterium of claim 22, which comprises a nucleic acid molecule encoding a non-Listerial antigen.
34. The attenuated *Listeria* bacterium of claim 33, wherein the non-Listerial antigen is a tumor-associated antigen or derived from a tumor associated antigen.
35. The attenuated *Listeria* bacterium of claim 34, wherein the antigen is a tumor associated antigen or derived from a tumor associated antigen selected from the group consisting of mesothelin, sp17, PAGE-4, gp-100, PSMA, K-ras, TARP, proteinase 3, WT-1, NY-ESO-1, CEA, Her-2, and SPAS-1.
36. The attenuated *Listeria* bacterium of claim 33, wherein the non-Listerial antigen is an infectious disease antigen or is derived from an infectious disease antigen.
37. An immunogenic composition comprising the attenuated *Listeria* bacterium of claim 22.
38. A vaccine comprising (a) the attenuated *Listeria* bacterium of claim 22, and (b) a pharmaceutically acceptable carrier or an adjuvant.
39. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of a composition comprising the attenuated *Listeria* bacterium of claim 22, wherein the attenuated *Listeria* bacterium comprises a nucleic acid encoding the antigen.

40. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a composition comprising the attenuated *Listeria* bacterium of claim 22.
41. A professional antigen-presenting cell comprising the attenuated *Listeria* bacterium of claim 22.
42. A strain selected from the group consisting of a *Listeria monocytogenes* $\Delta actA \Delta inlB$ strain deposited with the American Type Culture Collection (ATCC) and identified by accession number PTA-5562, or a mutant of the deposited strain which is defective both with respect to internalin B and ActA.
43. The strain of claim 42, which is the *Listeria monocytogenes* strain deposited with the American Type Culture Collection (ATCC) and identified by accession number PTA-5562.
44. An immunogenic composition comprising the strain of claim 42.
45. A vaccine comprising (a) the strain of claim 42, and (b) a pharmaceutically acceptable carrier or adjuvant.
46. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of a composition comprising the strain of claim 42, wherein the strain comprises a nucleic acid molecule encoding the antigen.
47. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of a composition comprising the strain of claim 42.
48. A professional antigen-presenting cell comprising the strain of claim 42.

49. A vaccine comprising (a) a *Listeria* bacterium, wherein the attenuated *Listeria* bacterium is attenuated for entry into non-phagocytic cells, and (b) a pharmaceutically acceptable carrier or an adjuvant.

50. The vaccine of claim 49, wherein the attenuated *Listeria* bacterium is defective with respect to one or more internalins.

51. The vaccine of claim 49, wherein the attenuated *Listeria* bacterium is defective with respect to internalin B.

52. The vaccine of claim 49, wherein the attenuated *Listeria* bacterium comprises a mutation in the *inlB* gene.

53. The vaccine of claim 49, wherein the attenuated *Listeria* bacterium belongs to the species *Listeria monocytogenes*.

54. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of the vaccine of claim 49.

55. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of the vaccine of claim 49, wherein the attenuated *Listeria* bacterium comprises a nucleic acid molecule encoding the antigen.

56. A isolated professional antigen-presenting cell comprising a *Listeria* bacterium, wherein the *Listeria* bacterium is attenuated for entry into non-phagocytic cells.

57. A method of inducing an immune response in a host to an antigen comprising administering to the host an effective amount of the professional antigen-presenting cell of claim 56, wherein the attenuated *Listeria* bacterium comprises a nucleic acid encoding the antigen.

58. A method of preventing or treating a disease in a host, comprising administering to the host an effective amount of the professional antigen-presenting cell of claim 56.

59. A method of inducing MHC class I antigen presentation or MHC class II antigen presentation on an antigen-presenting cell, comprising contacting a *Listeria* bacterium with an antigen-presenting cell, wherein the *Listeria* bacterium is attenuated for entry into non-phagocytic cells and comprises a nucleic acid molecule encoding a non-Listerial antigen comprising an MHC class I epitope or an MHC class II epitope.

60. A method of inducing an immune response in a host to an antigen, comprising the following steps: (a) contacting a *Listeria* bacterium with an antigen-presenting cell from the host, wherein the *Listeria* bacterium is attenuated for entry into non-phagocytic cells and comprises a nucleic acid molecule encoding the antigen; and (b) administering the antigen-presenting cell to the host.